

AMENDMENTS

In the claims:

Please cancel claims 39, 45, and 51, and amend the pending claims as follows:

1-15 (Cancelled)

16. (Currently Amended) A method for directing the biodistribution of a drug that binds to a protein target, wherein the drug is directed to an intracellular space upon administration to a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons consisting of a drug moiety comprising said drug or an active derivative thereof and a targeting moiety to an intracellular biodistribution modulating protein optionally joined by a linking group, wherein said drug moiety binds to a protein target and said targeting moiety **is a peptidyl-prolyl isomerase ligand** ~~has an affinity for its intracellular biodistribution modulating protein of at least about 10^{-6} M~~, and wherein said bifunctional molecule has a modulated biodistribution upon administration to said mammalian host as compared to a free drug control;

to direct said biodistribution of said drug upon administration to said host to an intracellular space as compared to a free drug control.

17. (Previously Presented) The method according to Claim 16, wherein said bifunctional molecule exhibits enhanced efficacy upon administration to said mammalian host as compared to a free drug control.

18. (Previously Presented) The method according to Claim 16, wherein said bifunctional molecule exhibits reduced toxicity upon administration to said mammalian host as compared to a free drug control.

19 - 21. (Cancelled)

22. **(Previously Presented)** The method according to Claim 16, wherein said bifunctional molecule comprises a linking group.

23. **(Previously Presented)** The method according to Claim 16, wherein said bifunctional molecule is administered as a pharmaceutical preparation.

24. **(Currently Amended)** A method for targeting a drug to an intracellular site of a mammalian host, said method comprising:

administering to said mammalian host an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons consisting of a drug moiety and a targeting moiety optionally joined by a linking group, wherein said drug moiety and targeting moiety bind to intracellular proteins and said targeting moiety is a peptidyl-prolyl isomerase ligand ~~has an affinity for its intracellular protein of at least about 10^{-6} M~~, and wherein said bifunctional molecule exhibits a modulated biodistribution upon administration to a mammalian host as compared to a free drug control;

to target said drug to an intracellular site of a mammalian host.

25. **(Original)** The method according to Claim 24, wherein said bifunctional molecule comprises a linking group.

26. **(Original)** The method according to Claim 24, wherein said bifunctional molecule does not include a linking group.

27-29. **(Canceled)**

30. **(Currently Amended)** In a method of administering a drug to a host in need of said drug, the improvement comprising:

administering to said host an effective amount of a bifunctional molecule having a molecular weight that does not exceed about 5000 daltons and consisting of said drug moiety comprising said drug or a derivative thereof covalently linked, either directly or through an optional linking group, to a targeting moiety that binds to an intracellular biodistribution modulating protein, wherein said drug moiety binds to an intracellular protein and said targeting moiety **is a peptidyl-prolyl isomerase ligand** ~~has an affinity for its intracellular biodistribution modulating protein of at least about 10^{-6} M.~~

31. **(Previously Presented)** The method according to Claim 30, wherein said host is a mammalian host.

32. **(Previously Presented)** The method according to Claim 31, wherein said mammalian host is human.

33. **(Original)** The method according to Claim 30, wherein said drug is a small molecule.

34. **(Original)** The method according to Claim 30, wherein said targeting moiety binds to an endogenous biodistribution modulating protein.

35. **(Cancelled)**

36. **(Original)** The method according to Claim 34, wherein said endogenous biodistribution modulating protein is an intracellular protein.

37-39 **(Cancelled)**

40. **(Currently Amended)** The method according to ~~Claim 39~~ **Claim 16**, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

41. **(Currently Amended)** The method according to ~~Claim 40~~ **Claim 16**, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

42. **(Currently Amended)** The method according to Claim 41, wherein said ~~peptidyl-prolyl isomerase~~ ligand **for an FKBP** is selected from the group consisting of FK506 and rapamycin.

43. **(Currently Amended)** The method according to ~~Claim 39~~ **Claim 16**, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

44. **(Currently Amended)** The method according to Claim 43, wherein said ~~peptidyl-prolyl isomerase~~ ligand **for a cyclophilin** is a cyclosporin.

45. **(Cancelled)**

46. **(Currently Amended)** The method according to ~~Claim 45~~ **Claim 24**, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

47. **(Currently Amended)** The method according to ~~Claim 46~~ **Claim 24**, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

48. **(Currently Amended)** The method according to Claim 47, wherein said ~~peptidyl-prolyl isomerase~~ ligand **for an FKBP** is selected from the group consisting of FK506 and rapamycin.

49. **(Currently Amended)** The method according to ~~Claim 46~~ **Claim 24**, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

50. **(Currently Amended)** The method according to Claim 49, wherein said ~~peptidyl-prolyl isomerase~~ ligand for a cyclophilin is a cyclosporin.

51. **(Cancelled)**

52. **(Currently Amended)** The method according to ~~Claim 51~~ Claim 30, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP or cyclophilin.

53. **(Currently Amended)** The method according to ~~Claim 52~~ Claim 30, wherein said peptidyl-prolyl isomerase ligand is a ligand for an FKBP.

54. **(Currently Amended)** The method according to Claim 53, wherein said ~~peptidyl-prolyl isomerase~~ ligand for an FKBP is selected from the group consisting of FK506 and rapamycin.

55. **(Currently Amended)** The method according to ~~Claim 53~~ Claim 30, wherein said peptidyl-prolyl isomerase ligand is a ligand for a cyclophilin.

56. **(Currently Amended)** The method according to Claim 55, wherein said ~~peptidyl-prolyl isomerase~~ ligand for a cyclophilin is a cyclosporin.